Medical Policy

Preimplantation Genetic Testing

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Policy Number: 088
BCBSA Reference Number: 4.02.05
NCD/LCD: N/A

Related Policies
Infertility Diagnosis and Treatment, #086

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Preimplantation genetic diagnosis (PGD)
Preimplantation genetic diagnosis (PGD) may be MEDICALLY NECESSARY including IVF with or without ICSI, even if the member is not infertile, when ALL of the following criteria are met:

1. The member has undergone genetic counseling, AND
2. The member has a > 5% chance of live birth per cycle of IVF with or without ICSI, AND
3. PGD is for evaluation of an embryo at an identified elevated risk for one of the following:
   a. A genetic disorder that is associated with severe disability or has a lethal natural history, such as when:
      i. Both partners are known carriers of a single gene autosomal recessive disorder,
      ii. One partner is a known carrier of a single gene autosomal recessive disorder and the partners have one offspring that has been diagnosed with that recessive disorder,
      iii. One partner is a known carrier of a single gene autosomal dominant disorder, or
      iv. One partner is a known carrier of a single X-linked disorder.
   b. A structural chromosomal abnormality such as for a parent with balanced or unbalanced chromosomal translocation.

Preimplantation genetic diagnosis (PGD) in conjunction with IVF is INVESTIGATIONAL in patients/couples who are undergoing IVF in all situations other than those specified above.

Examples of MEDICALLY NECESSARY diagnoses include but are not limited to the following:
### Single gene autosomal recessive disorders
- B-Thalessemia Syndromes
- Canavan Disease
- Cystic Fibrosis
- Epidermolysis Bullosa Simplex (autosomal recessive type)
- Fanconi Anemia
- Familial Dysautonomia
- Gaucher Disease
- Hurler Syndrome
- Metabolic disorders (e.g., methylmalonic acidemia or propionic acidemia)
- Sickle Cell Anemia
- Spinal Muscular Atrophy Type I
- Spinal cerebellar Ataxia (autosomal recessive type)
- Tay-Sachs Disease

### Single gene autosomal dominant disorders
- Epidermolysis Bullosa (autosomal dominant type)
- Huntington’s Disease
- Marfan's Syndrome
- Myotonic Dystrophy
- Neurofibromatosis Type I & II
- Retinoblastoma
- Spinal cerebellar Ataxia (autosomal dominant type)
- Tuberous Sclerosis

### Single gene x-linked recessive disorders
- Adrenoleukodystrophy
- Alport Syndrome
- Choroideremia
- Fabry’s Disease
- Fragile X Syndrome
- Hemophilia A & B
- Hunter Syndrome
- Incontinentia pigmanti
- Lesch-Nyhan Syndrome
- Muscular Dystrophy
- X-linked Mental Retardation

Preimplantation genetic diagnosis in conjunction with in vitro fertilization (IVF) in couples not known to be infertile may be considered **MEDICALLY NECESSARY** when used to evaluate human leukocyte antigen (HLA) status alone in families with a child with a bone marrow disorder requiring a stem cell transplant, and in whom there is no other source of a compatible bone marrow donor other than an HLA matched sibling.

**Preimplantation genetic screening (PGS)**
Preimplantation genetic screening (PGS) in conjunction with IVF is **INVESTIGATIONAL** in patients/couples who are undergoing IVF in all situations.

**Preimplantation genetic testing (PGT)**
Preimplantation genetic testing for a parent with a documented history of aneuploidy in a previous pregnancy is **INVESTIGATIONAL**.¹

**Prior Authorization Information**
Pre-service approval is required for all inpatient services for all products.
See below for situations where prior authorization may be required or may not be required for outpatient services.

| Commercial Managed Care (HMO and POS) | Yes |
| Commercial PPO and Indemnity | Yes |
| Medicare HMO Blue℠ | Yes |
| Medicare PPO Blue℠ | Yes |

**CPT Codes / HCPCS Codes / ICD Codes**
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.
Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

### CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>89290</td>
<td>Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos</td>
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<tr>
<td>89291</td>
<td>Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos</td>
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</tbody>
</table>

**Description**

Preimplantation genetic testing (PGT) involves analysis of biopsied cells as part of an assisted reproductive procedure. It is generally considered to be divided into two categories:

- Preimplantation genetic diagnosis (PGD) is used to detect a specific inherited disorder and aims to prevent the birth of affected children in couples at high risk of transmitting a disorder.
- Preimplantation genetic screening (PGS) uses similar techniques to screen for potential genetic abnormalities in conjunction with in vitro fertilization for couples without a specific known inherited disorder.

Preimplantation genetic testing (PGT) describes a variety of adjuncts to an assisted reproductive procedure in which either maternal or embryonic DNA is sampled and genetically analyzed, thus permitting deselection of embryos harboring a genetic defect prior to implantation of the embryo into the uterus. The ability to identify preimplantation embryos with genetic defects before the initiation of pregnancy provides an attractive alternative to amniocentesis or chorionic villus sampling (CVS), with selective pregnancy termination of affected fetuses.

Two different sources of genetic material may be sampled in PGT; either the first or second polar body of the oocyte may be sampled which focuses on maternal chromosomal abnormalities or the preimplantation embryo may be biopsied to detect genetic abnormalities arising from the maternal or paternal genetic material.

The biopsied material can be analyzed in a variety of ways. Polymerase chain reaction (PCR) or other amplification techniques can be used to amplify the harvested DNA with subsequent analysis for single genetic defects. This technique is most commonly used when the embryo is at risk for a specific genetic disorders such as Tay Sachs disease or cystic fibrosis. Fluorescent in situ hybridization (FISH) is a technique that allows direct visualization of specific (but not all) chromosomes to determine the number or absence of chromosomes. This technique is most commonly used to screen for aneuploidy, gender determination or to identify chromosomal translocations. FISH cannot be used to diagnose single genetic defect disorders. However, molecular techniques can be applied with FISH (such as microdeletions and duplications) and thus, single-gene defects can be recognized with this technique.

Another approach that is becoming more common is array comparative genome hybridization (CGH) testing at either the 8-cell or more often, the blastocyst stage. Unlike FISH analysis, this allows for 24 chromosome aneuploidy screening, as well as more detailed screening for unbalanced translocations and inversions and other types of abnormal gains and losses of chromosomal material.

Three general categories of embryos have undergone PGT:

1. **Embryos at risk for a specific inherited single genetic defect**
Inherited single-gene defects fall into 3 general categories: autosomal recessive, autosomal dominant, and X-linked. When either the mother or father is a known carrier of a genetic defect, embryos can undergo PGD to deselect embryos harboring the defective gene. Gender selection of a female embryo is another strategy when the mother is a known carrier of an X-linked disorder for which there is not yet a specific molecular diagnosis. The most common example is female carriers of fragile X syndrome. In this scenario, PGD is used to deselect male embryos, half of which would be affected. PGD could also be used to deselect affected male embryos. While there is a growing list of single genetic defects for which molecular diagnosis is possible, the most common indications include cystic fibrosis, beta thalassemia, muscular dystrophy, Huntington's disease, hemophilia, and fragile X disease. It should be noted that when PGD is used to deselect affected embryos, the treated couple is not technically infertile but are undergoing an assisted reproductive procedure for the sole purpose of PGD. In this setting, PGD may be considered an alternative to selective termination of an established pregnancy after diagnosis by amniocentesis or chorionic villus sampling.

2. Embryos at a higher risk of translocations
Balanced translocations occur in 0.2% of the neonatal population but at a higher rate in infertile couples or in those with recurrent spontaneous abortions. PGD can be used to deselect those embryos carrying the translocations, thus leading to an increase in fecundity or a decrease in the rate of spontaneous abortion.

3. Identification of aneuploid embryos
Implantation failure of fertilized embryos is a common cause for failure of assisted reproductive procedures; aneuploidy of embryos is thought to contribute to implantation failure and may also be the cause of recurrent spontaneous abortion. The prevalence of aneuploid oocytes increases in older women. These age-related aneuploidies are mainly due to nondisjunction of chromosomes during maternal meiosis. Therefore, PGS of the extruded polar bodies from the oocyte has been explored as a technique to deselect aneuploid oocytes in older women. The FISH technique is most commonly used to detect aneuploidy.

Summary
Preimplantation genetic testing has been shown to be technically feasible in detecting single gene defects, structural chromosomal abnormalities, and aneuploid embryos using a variety of biopsy and molecular diagnostic techniques. Ultimately, the choice is one of the risks (both medical and psychological) of undergoing IVF with PGD, compared to the option of normal fertilization and pregnancy with the possibility of a subsequent elective abortion.

PGD is considered medically necessary, as noted in the policy statements, when the evaluation is focused on a known disease or disorder, and the decision to undergo PGD is made upon careful consideration of the risks and benefits. There is insufficient evidence that preimplantation genetic screening improves ongoing pregnancy and live birth rates; thus, preimplantation genetic screening as an adjunct to in vitro fertilization is considered investigational.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>10/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>1/2016</td>
<td>Clarified medical necessity criteria. 1/1/2016.</td>
</tr>
<tr>
<td>11/2015</td>
<td>Clarified medical necessity criteria. 11/1/2015.</td>
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<tr>
<td>8/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>9/2015</td>
<td>Revised medical necessity language to include IVF for PGD and a list of covered diagnoses. Clarified language in investigational statements. Effective 9/1/2015.</td>
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<tr>
<td>9/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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</table>
2/2013  BCBSA National medical policy review.  
No change in medical policy statement. Effective 2/4/2013.

No changes to policy statements.

No changes to policy statements.

12/15/2010  Updated to add infertility treatment for a member with recurrent pregnancy loss in accordance with Massachusetts law (M.G.L.c. 175, section 47H and 211 C.M.R 37.09). Effective December 15, 2010.

Changes to policy statements.

No changes to policy statements.

10/2009  Revised to include benefit coverage information in the header section of the document that addresses infertility services when a healthy female member is age 35 or older and has not been able to conceive after a period of six months of actively trying.

No changes to policy statements.

1/2009  Updated to remove information regarding requirement of 3 FSH IUI prior to receiving IVF treatment for those that meet the definition of unexplained infertility; this change is effective January 2009 as published in the December '08 Provider Focus.

11/2008  BCBSA National medical policy review.  
Changes to policy statements.

No changes to policy statements.

2/2008  Policy edited with the removal of coverage references for preimplantation genetic diagnosis which is now addressed in a new medical policy document, #88.

No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

Endnotes

1 Based on ASRM guidelines